Claims

1. An oxidoreductase characterized in that it reduces a carbonyl compound to the corresponding (S)-hydroxy compound in the presence of NADH and water.

2. The oxidoreductase according to claim 1, characterized in that it is obtainable from yeasts of the genuses Pichia or Candida, in particular from Pichia capsulata.

3. The oxidoreductase according to claim 1 or 2, characterized in that it has the DNA-sequence according to SEQ ID NO: 8 and the amino acid sequence according to SEQ ID NO: 9.

4. The oxidoreductase according to one or several of claims 1 to 3, characterized in that more than 70% of the amino acids is identical to the amino acid sequence SEQ ID NO: 9 and that is has a specific activity of more than 1 µmol per mg protein, based on the reaction of ethyl-4-chloro-3-oxobutanoic acid to (R)-ethyl-4-chloro-3-hydroxybutanoic acid.

5. The oxidoreductase according to claim 4, characterized in that 80% to 99.5%, in particular 90% to 99.5%, especially 99% to 99.5%, are amino acids identical to the amino acid sequence of SEQ ID NO: 9.

6. The oxidoreductase according to one or several of claims 1 to 5, characterized in that it has an additional amount of 1 to 40 amino acids or 1 to 40 amino acids less than the oxidoreductase having the amino acid sequence SEQ ID NO: 9 and that it has a specific activity of more than 1 µmol per mg protein, based on the reaction of ethyl-4-chloro-3-oxobutanoic acid to (R)-ethyl-4-chloro-3-hydroxybutanoic acid.

7. The oxidoreductase according to claim 4, characterized in that 1 to 25 amino acids, in particular 2 to 20 amino acids, or 3 to 10 amino acids, more or less than in the amino acid sequence of SEQ ID NO: 9 are present.

8. The oxidoreductase according to one or several of claims 1 to 6, characterized in that it has the amino acid sequence of SEQ ID NO: 9 and is modified once, twice, three, four or five times by a water-soluble polymer and that the specific activity amounts to more than 1 µmol per mg protein, based on the reaction of ethyl-4-chloro-3-oxobutanoic acid to (R)-ethyl-4-chloro-3-hydroxybutanoic acid.

9. The oxidoreductase according to claim 8, characterized in that the water-soluble polymer is polyethylene glycol.

10. A protein fragment, characterized in that it represents fragments of the amino acid sequence SEQ ID NO: 9, having a number of 5 to 30 amino acids per fragment.

11. The protein fragment according to claim 10, characterized in that the fragments are fragments of SEQ ID NO: 9, having a chain length of 6 to 25 amino acids, in particular 8 to 20 amino acids or 10 to 18 amino acids, in particular of the amino acid sequence SEQ ID NO: 10.

12. A fusion protein, characterized in that it contains the oxidoreductase having the amino acid sequence SEQ ID NO: 9 or fragments of the amino acid sequence SEQ ID NO: 9, having a number of 5 to 30 amino acids which are connected via a peptide bond to a further polypeptide at the N-terminal or carboxy-terminal end.

13. An antibody, characterized in that it binds specifically to the oxidoreductase according to SEQ ID NO: 9 or SEQ ID NO: 10.

14. An isolated nucleic acid sequence which codes for the oxidoreductase according to SEQ ID NO: 9 and SEQ ID NO: 10.

15. An isolated DNA-sequence of the oxidoreductase which catalyzes the reduction of a carbonyl compound to the corresponding (S)-hydroxy compounds in the presence of NADH and water, wherein the DNA-sequence is selected from the group

a) DNA-sequence which has the nucleotide sequence according to SEQ ID NO: 8, SEQ ID NO: 5, SEQ ID NO: 6 or SEQ ID NO: 7, or the respective complementary strand thereof,

b) DNA-sequence which hybridizes to one or several of the DNA-sequences according to a) or to the complementary strands thereof, with the hybridization taking place unter stringent conditions, and

c) DNA-sequence which, as a result of the degeneration of the genetic code, encodes a protein which is encoded by one or several of the DNA-sequences according to a) or b).

16. An isolated DNA-sequence, characterized in that more than 70% of the nucleic acid bases is identical to the DNA-sequence according to SEQ ID NO: 8 or to the complementary strands thereof and that it encodes the oxidoreductase which has a specific activity of more than 1 μmol per mg protein, based on the reaction of ethyl-4-chloro-3-oxobutanoic acid to (R)-ethyl-4-chloro-3-hydroxybutanoic acid.

17. The isolated DNA-sequence according to claim 16, characterized in that 80% to 99.5%, in particular 90% to 99.5%, especially 99% to 99.5%, of the nucleic acid bases is identical to the DNA-sequence according to SEQ ID NO: 8.

18. An isolated DNA-sequence, characterized in that it is a nucleic acid sequence having 10 to 50 nucleic acid bases which has a sequence corresponding to a part or several parts of the DNA-sequence according to SEQ ID NO: 8 or to the complementary strands thereof.

19. The isolated DNA-sequence according to claim 18, characterized in that it is a nucleic acid sequence having 15 to 45 nucleic acid bases, in particular 20 to 40 bases or 30 to 40 nucleic acid bases.

20. A cloning vector, characterized in that it comprises one or several of the nucleic acid or DNA sequences according to claims 14 to 19.

21. An expression vector, characterized in that it comprises one or several of the nucleic acid or DNA sequences according to claims 14 to 19 and is linked in an appropriate manner to an expression control sequence.

22. A host cell which is a bacterial, yeast, insect, plant or mammalian cell and has been transformed or transfected with an expression vector according to claim 21.

23. A process for the enantioselective reduction of carbonyl compounds to the corresponding (S)-hydroxy compounds which is characterized in that

a) a carbonyl compound is reduced to the corresponding (S)-hydroxy compound in the presence of the oxidoreductase according to one or several of claims 1 to 9, NADH and water, and

b) the chiral (S)-hydroxy compound formed is isolated.

24. The process according to claim 23, characterized in that a compound of Formula I

R1-C(O)-R2 (I)

is used as a carbonyl compound, comprising a moiety R1 from

1) -(C_1-C_{20})-alkyl, wherein alkyl is linear-chain or branched,
2) -(C_2-C_{20})-alkenyl, wherein alkenyl is linear-chain or branched and contains one, two, three or four double bonds, depending on the chain length,
3) -(C_2-C_{20})-alkynyl, wherein alkynyl is linear-chain or branched and optionally contains one, two, three or four triple bonds,
4) -(C_6-C_{14})-aryl,
5) -(C_1-C_8)-alkyl-(C_6-C_{14})-aryl,
6) -(C_5-C_{14})-heterocycle which is unsubstituted or substituted one to three times by halogen, hydroxyl, amino or nitro, or
7) -(C_3-C_7)-cycloalkyl,

wherein the moieties R1 mentioned under 1) to 7) are unsubstituted or substituted one, two or three times, independently of each other, by

a) -OH,
b) halogen such as fluorine, chlorine, bromine or iodine,
c) -NO_2 or
d) -NH_2 and

comprising a moiety R2 from

1) -(C_1-C_6)-alkyl, wherein alkyl is linear-chain or branched,
2) -(C_2-C_6)-alkenyl, wherein alkenyl is linear-chain or branched and contains one, two or three double bonds, depending on the chain length,
3) -(C_2-C_6)-alkynyl, wherein alkynyl is linear-chain or branched and optionally contains one or two triple bonds, or
4) -(C_0-C_{10})-alkyl-C(O)-O-(C_1-C_6)-alkyl, wherein alkyl is linear or branched and is unsubstituted or substituted one to three times by halogen, hydroxyl, amino or nitro,

wherein the moieties R2 mentioned under 1) to 4) are unsubstituted or substituted one, two or three times, independently of each other, by

a) -OH,
b) halogen such as fluorine, chlorine, bromine or iodine,
c) -NO_2 or

d) $-NH_2$.

25. The process according to claim 23 or 24, characterized in that

a) a carbonyl compound is reduced to the corresponding (S)-hydroxy compound in the presence of the oxidoreductase according to one or several of claims 1 to 9, NADH and water,
b) the NAD formed by the oxidoreductase is reduced to NADH with a cosubstrate, and
c) the chiral (S)-hydroxy compound formed is isolated.

26. The process according to claim 23 or 24, characterized in that

a) a carbonyl compound is reduced to the corresponding (S)-hydroxy compound in the presence of the oxidoreductase according to one or several of claims 1 to 9, NADH and water,
b) the NAD formed by the oxidoreductase is reduced to NADH with a dehydrogenase and a cosubstrate, and
c) the chiral (S)-hydroxy compound formed is isolated.

27. The process according to claim 23 or 24, characterized in that

a) a carbonyl compound is reduced to the corresponding (S)-hydroxy compound in the presence of the oxidoreductase according to one or several of claims 1 to 9, NADH and water,
b) the reactions are carried out in the presence of an organic solvent, and
c) the chiral (S)-hydroxy compound formed is isolated.

28. The process according to claim 23 or 24, characterized in that

a) a carbonyl compound is reduced to the corresponding (S)-hydroxy compound in the presence of the oxidoreductase according to one or several of claims 1 to 9, NADH and water,
b) the reactions are carried out in the presence of an organic solvent,
c) the NAD formed by the oxidoreductase is reduced to NADH with a cosubstrate, and
d) the chiral (S)-hydroxy compound formed is isolated.

29. The process according to claim 23 or 24, characterized in that

a) a carbonyl compound is reduced to the corresponding (S)-hydroxy compound in the presence of the oxidoreductase according to one or several of claims 1 to 9, NADH and water,
b) the NAD formed by the oxidoreductase is simultaneously reduced to NADH with a dehydrogenase and a cosubstrate,
c) the reactions are carried out in the presence of an organic solvent, and
d) the chiral (S)-hydroxy compound formed is isolated.

30. The process according to claim 25, 26, 28 or 29, characterized in that ethanol, 2-propanol, 2-butanol, 2-pentanol or 2-octanol is used as the cosubstrate.

31. The process according to claim 26 or 29, characterized in that baker's yeast from Candida boidinii or Candida parapsilosis is used as the dehydrogenase.

32. The process according to claim 26 or 29, characterized in that NADH-dependent formate dehydrogenase is used as the dehydrogenase and a salt of formic acid such as ammonium formate, sodium formate or calcium formate is used as the cosubstrate.

33. The process according to claim 27 or 29, characterized in that diethyl ether, tertiary butyl methyl ether, diisopropyl ether, dibutyl ether, butyl acetate, heptane, hexane or cyclohexane is used as organic solvents.

34. The process according to claim 27 or 29, characterized in that the organic phase makes up 5% to 80% of the total reaction volume, preferably 10% to 40%.

35. A process for the recovery of chiral (R)-hydroxy compounds of Formula II,

R1-C(OH)-R2 (II)

comprising a moiety R1 from

1) -(C_1-C_{20})-alkyl, wherein alkyl is linear-chain or branched,
2) -(C_2-C_{20})-alkenyl, wherein alkenyl is linear-chain or branched and contains one, two, three or four double bonds, depending on the chain length,

3) -(C_2-C_{20})-alkynyl, wherein alkynyl is linear-chain or branched and optionally contains one, two, three or four triple bonds,
4) -(C_6-C_{14})-aryl,
5) -(C_1-C_8)-alkyl-(C_6-C_{14})-aryl,
6) -(C_5-C_{14})-heterocycle which is unsubstituted or substituted one to three times by halogen, hydroxyl, amino or nitro, or
7) -(C_3-C_7)-cycloalkyl,

wherein the moieties R1 mentioned under 1) to 7) are unsubstituted or substituted one, two or three times, independently of each other, by

a) -OH,
b) halogen such as fluorine, chlorine, bromine or iodine,
c) -NO_2 or
d) -NH_2 and

comprising a moiety R2 from

1) -(C_1-C_6)-alkyl, wherein alkyl is linear-chain or branched,
2) -(C_2-C_6)-alkenyl, wherein alkenyl is linear-chain or branched and contains one, two or three double bonds, depending on the chain length,
3) -(C_2-C_6)-alkynyl, wherein alkynyl is linear-chain or branched and optionally contains one or two triple bonds, or
4) -(C_0-C_{10})-alkyl-C(O)-O-(C_1-C_6)-alkyl, wherein alkyl is linear or branched and is unsubstituted or substituted one to three times by halogen, hydroxyl, amino or nitro,

wherein the moieties R1 mentioned under 1) to 4) are unsubstituted or substituted one, two or three times, independently of each other, by

a) -OH,
b) halogen such as fluorine, chlorine, bromine or iodine,
c) -NO_2 or
d) -NH_2,

characterized in that

a) a mixture containing the racemic compound of Formula II is incubated with the oxidoreductase according to one or several of claims 1 to 9, NAD and water, and

b) the remaining chiral (R)-hydroxy compound of Formula II is isolated.

36. The process for the recovery of chiral (R)-hydroxy compounds of Formula II according to claim 35, characterized in that

a) a mixture containing the racemic compound of Formula II is incubated with the oxidoreductase according to one or several of claims 1 to 9, NAD and water,
b) the NADH formed by the oxidoreductase is oxidized to NAD with a cosubstrate, and
c) the remaining chiral (R)-hydroxy compound of Formula II is isolated.

37. The process for the recovery of chiral (R)-hydroxy compounds of Formula II according to claim 35, characterized in that

a) a mixture containing the racemic compound of Formula II is incubated with the oxidoreductase according to one or several of claims 1 to 9, NAD and water,
b) the NADH formed by the oxidoreductase is oxidized to NAD with a dehydrogenase and a cosubstrate, and
c) the remaining chiral (R)-hydroxy compound of Formula II is isolated.

38. The process for the recovery of chiral (R)-hydroxy compounds of Formula II according to claim 35, characterized in that

a) a mixture containing the racemic compound of Formula II is incubated with the oxidoreductase according to one or several of claims 1 to 9, NAD and water,
b) the reactions are carried out in the presence of an organic solvent, and
c) the remaining chiral (R)-hydroxy compound of Formula II is isolated.

39. The process for the recovery of chiral (R)-hydroxy compounds of Formula II according to claim 35, characterized in that

a) a mixture containing the racemic compound of Formula II is incubated with the oxidoreductase according to one or several of claims 1 to 9, NAD and water,

b) the reactions are carried out in the presence of an organic solvent,

c) the NADH formed by the oxidoreductase is oxidized to NAD with a dehydrogenase and a cosubstrate, and

d) the remaining chiral (R)-hydroxy compound of Formula II is isolated.

40. The process according to claim 36, 37 or 39, characterized in that acetone is used as the cosubstrate.